PATENT
Atty. Docket: 030639.0044.CPA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Duft, et al.

Serial No.: 09/445,517

Filed: December 6, 1999

Title: METHODS FOR TREATING OBESITY

Group Art Unit: 1645

Examiner: S. Devi

DECLARATION UNDER 37 C.F.R. § 1.131

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

1. Having reviewed the June 5, 2002 Office Action in the above-captioned case, we understand that pending claims 1-14 in the subject patent application have been rejected by the U.S. Patent and Trademark Office ("PTO") for alleged lack of novelty in view of an Abstract bearing the date "May 1997" (Thompson *et al.*, *Diabetes*, 46(Supp. 1):30A). A copy of this document, which was included in an Abstract Book for the 57th Scientific Sessions of the American Diabetes Association (the "ADA," publisher of *Diabetes*) in Boston, MA on June 21-24, 1997, is attached hereto as Exhibit A and is hereinafter referred to as the "Thompson/Pearson/Schoenfeld/Kolterman Abstract."

2. The Thompson/Pearson/Schoenfeld/Kolterman Abstract describes clinical experiments undertaken by Amylin Pharmaceuticals. All of the named authors, Robert Thompson, Leeanne Pearson, and Steven Schoenfeld, as well as Dr. Kolterman, were employees of Amylin Pharmaceuticals, Inc. at the time the experiments described therein were planned and

carried out, prior to its publication, including experiments designed and supervised by Dr. Kolterman relating to weight loss.

3. Assuming for the purposes of this Declaration the assertion of the Patent Office that claims 1-14 of the present application first filed on June 6, 1997 were anticipated by the Thompson/Pearson/Schoenfeld/Kolterman Abstract, we thus note that the information referenced in the Thompson/Pearson/Schoenfeld/Kolterman Abstract relates to work done under the direction and supervision of one of the undersigned co-inventors, Dr. Orville Kolterman at Amylin Pharmaceuticals, who is also its co-author.

4. Attached Exhibits B, C, and D demonstrate, furthermore, that the subject matter of the Thompson/Pearson/Schoenfeld/Kolterman Abstract relied on by the PTO was based on a reduction to practice of the subject matter thereof not later than January 6, 1997.

5. A copy of the Abstract Preparation Guidelines governing submission of this Abstract to the ADA for the 57th Scientific Sessions is attached hereto as Exhibit B, showing that the Thompson/Pearson/Schoenfeld/Kolterman Abstract was prepared prior to January 6, 1997, and submitted to the ADA on or before January 6, 1997, for the 57th Scientific Sessions in Boston, MA on June 21-24, 1997. As evidenced by Exhibit B, the ADA required that abstracts be received by January 6, 1997 in order to be published in the Abstract Book for the 57th Annual Meeting. Paragraph 33 in the Exhibit B Abstract Preparation Guidelines specified that any abstracts submitted after January 6, 1997 were deemed "late-breaking research" abstracts that would "not be published in the Abstract Book" nor "appear in the Final Program because of printing deadlines." As specified in Paragraph 7 of Exhibit B, the ADA did not permit changes to submitted Abstracts.

6. Attached as Exhibit C is a copy of the Abstract Submission form that accompanied the Thompson/Pearson/Schoenfeld/Kolterman Abstract submitted to and received by the ADA on or before January 6, 1997. As evidenced by Exhibit C, the Thompson/Pearson/Schoenfeld/Kolterman Abstract was not submitted as a "late-breaking research" abstract. Thus, in accordance with the Exhibit B Abstract Preparation Guidelines, it was included in the May 1997 *Diabetes* Abstract Book cited by the PTO. Further, the content of Abstract submitted to the ADA (Exhibit C) is the same as the published Abstract bearing the date "May 1997" (Thompson *et al.*, *Diabetes*, 46(Supp. 1):30A) (Exhibit A).

7. Attached as Exhibit D is a letter of acceptance from the ADA to Robert Thompson dated March 17, 1997, establishing that the Abstract submitted to and received by the ADA on or before January 6, 1997 was reviewed and accepted for publication not latter March 17, 1997.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 101 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified U.S. Patent Application or any Patent issued thereon.

Dated: December 3, 2002

Orville G. Kolterman, M.D.

Dated: December 5, 2002

Bradford J. Duft

EXHIBIT A

MAY 1997 VOLUME 46 SUPPLEMENT 1

diabetes

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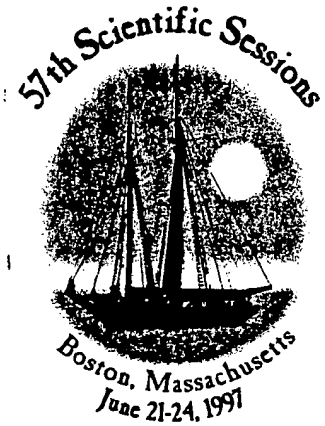
www.diabetes.org/diabetes



ABSTRACT BOOK

57th Annual Meeting and Scientific Sessions

Saturday, June 21 — Tuesday, June 24, 1997

Hynes Convention Center
Boston, Massachusetts

DIAEAZ 46 Supplement (1) 1A–434 (1997)
ISSN 0012-1797

0116

Pramlintide, an Analog of Human Amylin Improves Glycemic Control in Patients with Type II Diabetes Requiring Insulin.

ROBERT THOMPSON*[1], LEEANNE PEARSON*[1], STEVEN SCHOENFELD*[1], ORVILLE KOLTERMAN*[1]. *San Diego, CA*

The effects of 4 weeks of subcutaneous administration of pramlintide, (Pr) an analog of human amylin, on glycemic control in 203 patients with Type II diabetes mellitus requiring insulin were examined in a randomized, double-blind, placebo-controlled, parallel-group trial. Statistically significant reductions in serum fructosamine concentration were observed in the Pr 30 μg QID group (17.5±4.9 μmol/L), the Pr 60 μg TID group (24.1±4.9 μmol/L) and the Pr 60 μg QID group (22.6±4.1 μmol/L) compared to placebo (PBO) (3.5±3.8 μmol/L). There also were statistically significant shifts in the proportion of patients with an abnormal serum fructosamine concentration at baseline that normalized at Week 4 within the Pr 60 μg TID group (28%) and the Pr 60 μg QID group (31%) compared to PBO (10%). Consistent with the reduction in fructosamine, there were also statistically significant reductions in HbA_{1c} in the Pr 30 μg QID group (0.53±0.07%), the Pr 60 μg TID group (0.58±0.07%) and the Pr 60 μg QID group (0.51±0.08%) compared to placebo (0.27±0.08%). Based on RBC lifespan, and assuming stable glycemic control, these reductions in HbA1c in the Pr groups should increase over the following 2-3 months. The reductions in fructosamine and HbA_{1c} were accompanied by a statistically significant reduction in fasting total and LDL cholesterol. In contrast to treatment with insulin alone, there were trends towards decreased body weight in the Pr 60 μg TID and 60 μg QID groups. Furthermore, the incidence of hypoglycemia was no greater in any Pr group than in placebo. In conclusion, measurement of similar changes in both serum fructosamine concentration and HbA_{1c} suggests that pramlintide therapy for 28 days improves glycemic control in patients with Type II diabetes mellitus requiring insulin.

EXHIBIT B

NOVEMBER 1996 VOLUME 45 NUMBER 11

diabetes

A JOURNAL OF THE AMERICAN DIABETES ASSOCIATION®

Abstract Form for 57th Scientific Sessions Included; Submission Deadline Is January 6, 1997

PERSPECTIVES IN DIABETES

ORIGINAL ARTICLES

DIAEAZ 45(11) 1289–1454 (1996)
ISSN 0012-1797

►*Table of contents continues on page iii.*

American Diabetes Association.

57th SCIENTIFIC SESSIONS

June 21 - 24, 1997 Boston, MA

Submission Deadline: Monday, January 6, 1997

ABSTRACT PREPARATION GUIDELINES

GENERAL INFORMATION

1. Abstracts must be received at the Association's National Center by Monday, January 6, 1997.

2. Abstracts are not eligible if the paper has been presented at another national or international meeting or has been accepted for publication before the abstract submission deadline and will be published prior to the 57th Scientific Sessions. Failure to notify the Association of the publication of an abstract will result in a moratorium on the submission of abstracts for all authors appearing on the abstract in question for one year.

3. The printed abstract must be an original, submitted on the original abstract forms found in this packet. Abstracts cannot be submitted via fax.

4. An individual (member or non-member) may appear on four abstracts as an author, but may only appear as first author on two abstracts. A member may appear as author, co-author, or sponsor. A non-member may appear as author or co-author, but not as a sponsor. Authors are not required to be members of the Association.

5. Originality of work, adequacy of data, and clarity of exposition are the determinants in the selection of abstracts. Make abstracts as informative as possible, including a brief statement of the purpose of the study or why it was done, the methods or what was done, the results observed, and the author(s)' conclusions based on the results. Actual data should be summarized. It is inadequate to state "The results will be discussed" or "The data will be presented." Tables may be used to present data (refer to #18 in the instructions)

6. The final decision with respect to selection, programming, and/or publication of any abstract will be made by the Association's Scientific Sessions Meeting Committee.

7. Accepted abstracts will be printed as submitted. Changes to abstracts will not be accepted after submission. They should be carefully written and edited prior to submission.

8. For additional abstract packets, or if you have questions about completing the abstract form, contact Sandy DeVault, American Diabetes Association, 1660 Duke Street, Alexandria, VA 22314-3447, USA; phone: 703/549-1500, ext. 2096; FAX: 703/683-1839; E-mail: sdevault@diabetes.org.

9. Oral presentations at the Scientific Sessions will be limited to ten minutes each to allow time for discussion.

10. Expenses associated with the submission and presentation of the abstract are the responsibility of the presenter.

11. Presenters must pay the registration fee for attendance at the Scientific Sessions. Presenters will be able to register at pre-registration rates. For more information on registration, contact the Meeting Services Department, American Diabetes Association, 1660 Duke Street, Alexandria, VA 22314-3447, USA; phone: (703) 549-1500, ext. 2453 or 2330; FAX: (703) 683-1351; E-mail: meetings@diabetes.org.

COMPLETING THE FORMS

12. Accepted abstracts will be reduced by 25% and photographed as submitted for publication in the 57th Abstract Book, the May supplement to *Diabetes*. We recommend using a font no smaller than 10 points.

13. The text must be clear, within the border of the form, and limited to the space provided. Use only a typewriter or laser printer, as the quality of dot matrix printers varies considerably. Those with text exceeding the border will not be accepted. Text glued or taped inside the border will be accepted. Please use the following tips when printing your abstract:

- If typed, use carbon ribbon or slightly used black silk ribbon (new ribbons smudge, old ones reproduce too faintly). Practice typing the abstract in a rectangle 4 3/16" (10.64 cm) X 6 3/16" (15.42 cm) before using the original form.
- If using a laser printer, please note that the page size of the form is not standard. A left margin of 1.15" (2.92 cm) and a right margin of 3.35" (8.51 cm) should keep the text within the border. Practice printing the abstract with these margins before using the original form.

14. Abstract headings must follow a specified format. The format is as follows (refer to the example below):

a. Headings should begin to the immediate right of the box located in the upper left corner of the abstract area.

b. The first letters of major words in the title should be capitalized. Do not use subtitles (e.g., Methods, Results) in the abstract body.

c. Author(s)' complete first and last name(s) should be listed and capitalized. Authors who appear on more than one abstract should list their names the same way on all.

d. Author(s) who are members of the Association's Professional Section must be indicated by an asterisk (*) after their name. No other identifying marks are permissible except as noted in "e." below.

e. Author(s) who indicate "yes" on the *Duality of Interest Disclosure Form* (see pg. 6) must include a notation after their name(s). Use the following to indicate the type of duality: 1= any significant financial interest or other relationship with the manufacturer(s) of any commercial product(s) and/or providers(s) of commercial services discussed in the educational presentation; 2 = any significant financial interest or other relationship with any commercial supporters of the activity.

f. Do not list credentials, degrees, academic title(s) (e.g., MD, RN, RD), departments, divisions, or institutional affiliation(s) on the abstract form.

g. Include city and state (postal abbreviations) or country of origin of work; do not include street address and zip code.

Example of abstract heading:

A Novel Form of Chelatin Prevents IDDM in BB Rats.
JOHN DOE[1], JAMES E. REASONER*, SUSAN SMITH[2], JANE FRIDAY[2], Alexandria, VA

15. The first line of the text of the abstract and first line of any subsequent paragraphs should be indented three spaces.

16. The use of standard abbreviations is requested. Examples include kg, g, mg, ml, L (liter), meq, m (meter), mM (millimoles per liter), / (per), and % (percent). Place special or unusual abbreviations in parentheses after the full word the first time it appears, then use the abbreviation throughout the rest of the abstract. Use numerals to indicate numbers, except when beginning sentences.

17. Nonproprietary (generic) names should be used the first time a drug is mentioned and typed in lowercase letters; names are always capitalized, for example, aspirin (Bufferin).

18. Simple tables or special symbols may be included if they fit within the border of the form. Material that cannot be typed should be drawn in India ink.

19. Do not include references, credits, or grant support information in the abstract.

20. The Scientific Sessions Meeting Committee will consider presentation preference when planning the program. An abstract marked as "Only" (see Forms, pages 3 and 5) indicates that the authors do not want an abstract considered for any other type of presentation. For example, if an abstract is marked as "Oral Only" and is not selected for an oral presentation, the committee will not place the abstract in a poster session. Marking an abstract as "Oral Only" will not guarantee its selection for the program.

21. Categories for the 57th Scientific Sessions are located on page 4. Indicate the appropriate category under which you wish to have the abstract reviewed on both Form A and Form B. The Scientific Sessions Meeting Committee reserves the right to move an abstract that has been inappropriately categorized without notifying the author(s).

22. The signature of an active member of the Professional Section of the American Diabetes Association is required to validate the abstract. Members who sponsor non-members should verify that the latter are conforming to the rules. A member is not limited to the number of abstracts he/she can sponsor.

23. All authors must read and sign the *Duality of Interest* form (page 6) and this form must be included with each abstract submitted. Please refer to #14e for instructions on noting dualities on the abstract form. When preparing abstracts, please allow enough time to have all authors sign the original form.

24. Provide the information requested for the corresponding author, who will receive notification of abstract status (#28).

25. If the research presented in this abstract has been supported, in whole or in part, by a grant from the American Diabetes Association, please indicate so by checking on the appropriate line. Accepted abstracts with Association funding will be highlighted in the Final Program of the 57th Scientific Sessions. The response provided to this question will not affect the acceptance of abstracts for the 57th Scientific Sessions.

26. Before mailing an abstract submission, use the checklist on page 7 to confirm that all instructions have been followed and all items have been included in the submission packet.

ACKNOWLEDGEMENT OF RECEIPT AND ABSTRACT STATUS

27. For acknowledgment that an abstract was received by the Association, you must provide a self-addressed, US stamped postal card addressed to the corresponding author. The reverse side of the card should indicate the title of the abstract. Confirmation of receipt cannot be made by phone.

28. A letter of notification and appropriate accompanying materials will be sent by mail to the corresponding author. In addition, all international correspondence will be sent by Internet E-mail or fax if the appropriate numbers are included on form A.

MAILING SUBMISSION

29. A non-refundable processing fee of US $35.00 and a completed payment form (see page 7) must accompany each abstract submitted to the American Diabetes Association. Payment must be in the form of a check or credit card. Checks must be in U.S. funds and drawn on a U.S. bank, and made payable to the *American Diabetes Association.* Major credit cards (American Express, VISA, MasterCard) are also accepted. Purchase orders and money orders will not be accepted.

30. The review of abstracts is blinded, therefore two forms must be submitted: one (1) for publication (Form A) with the title and author(s)' name(s) within the border of the form, and one (1) for review (Form B) without author information. Please refer to Abstract Forms A and B on pages 3 and 5 for further instructions.

31. Five (5) copies of the front only of each form must also be provided for processing.

32. Do not fold the originals or copies. They should be mailed FIRST CLASS or AIR MAIL, when applicable, and addressed as follows: Scientific Sessions Meeting Committee, American Diabetes Association, P.O. Box 26427, Alexandria, VA 22313-6427, USA. Abstracts sent by express mail should be addressed as follows: Scientific Sessions Meeting Committee, American Diabetes Association, 1660 Duke Street, Alexandria, VA 22314-3447, USA. When shipping express mail, do not ship for a Saturday arrival. **Abstracts submitted via fax will not be accepted for review.**

"LATE-BREAKING RESEARCH" ABSTRACTS

33. Late-breaking research abstracts will be peer-reviewed, and only those deemed **highly meritorious** will be accepted for presentation. Selected abstracts will be presented during the President's Poster Session. "Late-breaking research" abstracts will not be published in the Abstract Book, nor will they appear in the Final Program because of printing deadlines. Authors should use the forms and follow instructions found in this packet. The appropriate box on Form A must be check marked, and all submissions must be received by May 16, 1997. The processing fee for abstracts in this classification is $50. "Late-breaking research" abstracts must be sent to the attention of Sandy DeVault, American Diabetes Association, 1660 Duke Street, Alexandria, VA 22314-3447 USA. Notification of abstract status will be provided no later than May 30, 1997.

TYPE ABSTRACT WITHIN BOX

FOR OFFICE USE ONLY
Date Rec'd _____ PMT? _____
Abstract No. _____
Duality? ___ Y ___ N Signed? ___ Y ___ N
Record No. _____
Mean Score _____

American Diabetes Association.

FORM A
(For publication)

CHECK ONE (See #21):

- ☐ Poster Session Preferred
- ☐ Oral Session Preferred
- ☐ Poster Session Only
- ☐ Oral Only
- ☐ No Preference

The author's wishes will be followed if possible.

☐ I am submitting this abstract after January 6, 1997 as "late-breaking research" (See #33).

Abstract Category Number: _____
(Categories listed on pg 4)

IMPORTANT

This form must be signed by an active member of the Professional Section of the American Diabetes Association.

The instructions on pages 1 and 2 must be followed exactly for abstracts to be considered for review.

The sponsoring member agrees that the material submitted herein conforms with the instructions on pages 1 and 2.

_____
MEMBER SIGNATURE

_____
PRINTED NAME

List family name, first name, middle initial, credentials/degrees, address (including city/state/country/zip), and telephone/fax numbers of author who should receive correspondence (please type or print):

Family Name _____

First Name _____ MI _____

Credentials/Degrees _____ Department _____

Institution _____

Street Address _____

City _____ State _____ Country _____ Zip Code/Postal Code _____

Phones (include area code/country/city code): Work: _____ Fax: _____

Has this research been supported, in whole or in part, by a grant from the American Diabetes Association? ____Y____N

Internet E-mail address: _____ (International submitters must include for timely notification)

1348

EXHIBIT C

TYPE ABSTRACT WITHIN BOX

Pramlintide, an Analog of Human Amylin Improves Glycemic Control in Patients with Type II Diabetes Requiring Insulin.

ROBERT THOMPSON*[1],LEEANNE PEARSON*[1],STEVEN SCHOENFELD*[1], ORVILLE KOLTERMAN*[1]. San Diego, CA

The effects of 4 weeks of subcutaneous administration of pramlintide, (Pr) an analog of human amylin, on glycemic control in 203 patients with Type II diabetes mellitus requiring insulin were examined in a randomized, double-blind, placebo-controlled, parallel-group trial. Statistically significant reductions in serum fructosamine concentration were observed in the Pr 30 µg QID group (17.5±4.9 µmol/L), the Pr 60 µg TID group (24.1±4.9 µmol/L) and the Pr 60 µg QID group (22.6±4.1 µmol/L) compared to placebo (PBO) (3.5±3.8 µmol/L). There also were statistically significant shifts in the proportion of patients with an abnormal serum fructosamine concentration at baseline that normalized at Week 4 within the Pr 60 µg TID group (28%) and the Pr 60 µg QID group (31%) compared to PBO (10%). Consistent with the reduction in fructosamine, there were also statistically significant reductions in HbA_{1c} in the Pr 30 µg QID group (0.53±0.07%), the Pr 60 µg TID group (0.58±0.07%) and the Pr 60 µg QID group (0.51±0.08%) compared to placebo (0.27±0.08%). Based on RBC lifespan, and assuming stable glycemic control, these reductions in HbA1c in the Pr groups should increase over the following 2-3 months. The reductions in fructosamine and HbA_{1c} were accompanied by a statistically significant reduction in fasting total and LDL cholesterol. In contrast to treatment with insulin alone, there were trends towards decreased body weight in the Pr 60 µg TID and 60 µg QID groups. Furthermore, the incidence of hypoglycemia was no greater in any Pr group than in placebo. In conclusion, measurement of similar changes in both serum fructosamine concentration and HbA_{1c} suggests that pramlintide therapy for 28 days improves glycemic control in patients with Type II diabetes mellitus requiring insulin.

FOR OFFICE USE ONLY

Date Rec'd _____ PMT?_____

Abstract No. _____

Duality?____ Y ___N Signed?___ Y

Record No. _____

Mean Score _____

American Diabetes Association.

FORM A
(For publication)

CHECK ONE (See #21):

- ☐ Poster Session Preferred
- ☒ Oral Sessic Preferred
- ☐ Poster Session Only
- ☐ Oral Only
- ☐ No Preference

The author's wishes will be followed if po.

☐ I am submitting this abstract after January 6, 1997 as "late-breaking research" (See #33).

Abstract Category Number: 14
(Categories listed on pg 4)

IMPORTANT

This form must be signed by an active r ber of the Professional Section of the A can Diabetes Association.

The instructions on pages 1 and 2 mu followed exactly for abstracts to be consi for review.

The sponsoring member agrees that th terial submitted herein conforms witl instructions on pages 1 and 2.

Robert G. Thomps
MEMBER SIGNATURE

R. Thompson
PRINTED NAME

List family name, first name, middle initial, credentials/degrees, address (including city/state/country/zip), and telephone/fax numbers of author who should receive correspondence (please type or print):

Family Name Thompson

First Name Robert MI G

Credentials/Degrees M.D Department Clinical Development

Institution Amylin Pharmaceuticals

Street Address 9373 Towne Centre Dr

City San Diego State Ca Country U.S.A. Zip Code/Postal Code 92121

Phones (include area code/country/city code): Work: 619-642-7133 Fax: 619-554-1472

Accepted for Oral Presentation

in part, by a grant from the American Diabetes Association? ____Y X N

EXHIBIT D

American Diabetes Association®

National Center
1660 Duke Street
Alexandria, Virginia 22314
Tel: 703 549-1500
Fax:703 836-7439
http://www.diabetes.org

To prevent and cure diabetes

and to improve the lives of

all people affected by diabetes.

March 17, 1997

Robert G. Thompson, MD
Clinical Development
Amylen Pharmacenticals
9373 Towne Centre Dr.
San Diego, CA 92121

Dear Dr. Thompson:

Congratulations! It is a pleasure to inform you that your abstract, *Pramlintide, an Analog of Human Amylin Improves Glycemic Control in Patients with Type II Diabetes Requiring Insulin*, has been selected for presentation at the Scientific Sessions of our 57th Annual Scientific Meetings and Sessions to be in Boston, Massachusetts from June 21-24, 1997. Your abstract, No. 0116 , will also be published in the May 1997 supplement issue of *Diabetes*.

Your abstract was selected by the Scientific Sessions Meeting Committee from the over 1,500 abstracts submitted this year. It is currently scheduled to be presented as an oral presentation on Sunday, June 22 from 5:30-5:45 p.m. The room assignment has not been made yet, but will be shortly and we will forward that information to you.

Enclosed are appropriate instructions for your presentation and a Preliminary Program with registration and housing forms. Please complete the forms and return them as soon as possible to the address indicated. Since you will not receive this notification until after the March 14 pre-registration deadline, you will be allowed to register at the rate of $260 for Association members or $395 for non-members. Be sure to return your completed registration form by May 1. The registration form enclosed indicates that you are an abstract presenter.

In the event you are unable to attend the meeting due to unforeseen circumstances, please make arrangements to have a co-author present the abstract. If you are unable to make such arrangements or have any questions, contact Sandy DeVault, Manager, Professional Programs at 703/299-2096.

On behalf of the Scientific Sessions Meeting Committee, I would like to thank you for your contribution and effort.

Sincerely,

Dale L. Greiner, PhD
Chair
Scientific Sessions Meeting Committee

DG:sd
Enclosures